## REMARKS

Consideration and entry of this paper, reconsideration and withdrawal of the rejections of the July 3, 2007 Final Office Action, and withdrawal of Applicants' previously-filed Petition (as mentioned at pages 1-2 of this paper) are respectfully requested in view of the amendments and remarks herein, and the matters discussed among Drs. David Alcock and John Normanton, Ms. Angela Collison and SPE S. Padmanabhan on 2 October 2007, and among Drs. David Alcock and John Normanton, Ms. Angela Collison, SPE S. Padmanabhan, and Examiner Badio on 4 October 2007, for which the SPE and Examiner are thanked for the courtesies extended..

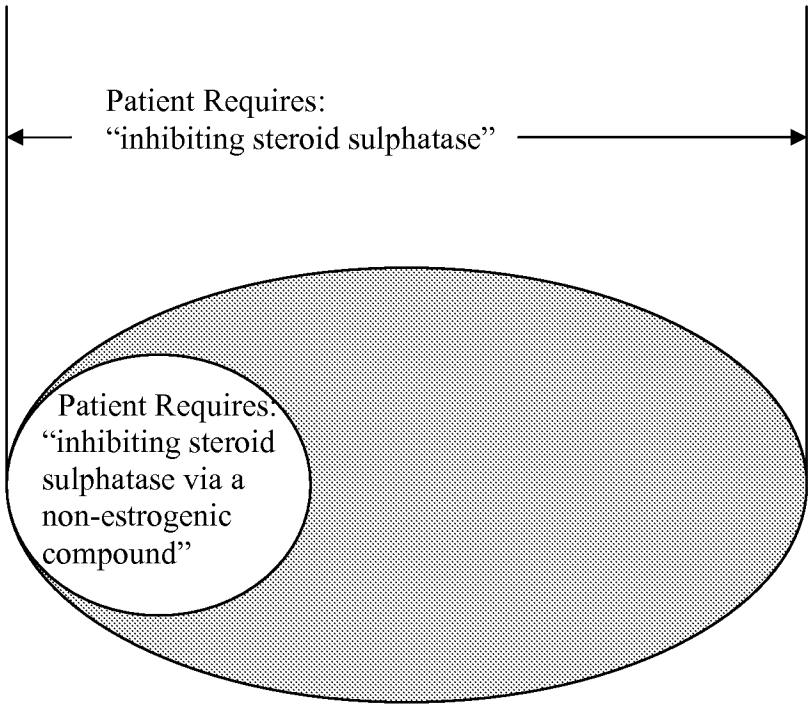
The claims are amended to be method claims as discussed during the interviews. No new matter is added. Furthermore, while Applicants ask that the previously-filed Petition be withdrawn, the arguments therein for why the previous double patenting rejections based upon US Patents Nos. 6,903,084 and 7,119,081 are hereby incorporated herein by reference; and, in re-opening prosecution, the Examiner and her SPE are asked to fully and carefully review those arguments and the case citation therein.

During the interview it was particularly discussed that the presently-claimed invention is not taught or suggested by the prior art and not taught or suggested by any claims of other patents or applications of Profs. Reed and Potter or assigned to Sterix Limited, and especially not taught or suggested by any claims of other patents or applications in any predecessor patents or applications of Profs. Reed and Potter or assigned to Sterix Limited.

In this regard, it was particularly discussed that the recitations of method claims 67 and 68 – "A method of inhibiting steroid sulphatase activity comprising administering, a non-oestrogenic sulphamate compound suitable for use as an inhibitor of oestrone sulphatase to a patient in need of inhibition of steroid sulphatase activity by a compound lacking oestrogenic activity, wherein the non-oestrogenic sulphamate compound is a sulphamate compound having Formula IV" and "A method of treating endocrine-dependent cancer comprising administering non-oestrogenic sulphamate compound suitable for use as an inhibitor of oestrone sulphatase, to a patient in need of treatment of endocrine-dependent cancer by a compound lacking oestrogenic activity, wherein the compound is a sulphamate compound having Formula IV" – breath life and

meaning into the claims and patentably distinguish from the prior art and the claims of other patents or applications of Profs. Reed and Potter or assigned to Sterix Limited.[1]

For example, with reference to claim 67 and the drawing below, while the prior art may involve the broad area of "inhibiting steroid sulphatase" (shaded grey in the below drawing), the present invention pertains to administering to a discreet subset thereof, namely the group that is in need of inhibition of steroid sulphatase (or in need of cancer treatment, with reference to claim 68) but with a non-oestrogenic compound (shaded white in the below drawing).




That is, the methods of claims 67 and 68 and the claims dependent thereon are directed to a particular, discreet group; and hence the methods are not taught or suggested by the prior art and are by any claims of other patents or applications of Profs. Reed and Potter or assigned to Sterix Limited.

[1] Furthermore, the recitations of the claims are well supported by the application text and claims as originally filed, including without limitation page 3, lines 19-23 *et seq.* ("[t]he term 'non-oestrogenic compound' … means a compound exhibiting no or substantially no oestrogenic activity … compounds may not be capable of being metabolized to compounds with display or induce hormonal activity"); Example 2, *in vivo* studies: oestrogenicity examined in ovariectomised rats; in this model compounds which are oestrogenic stimulate uterine growth); page 26 (oestrogens are major mitogens involved in promoting growth of tumors in endocrine-dependent tissues); page 30 (treatment of endocrine-dependent cancers such as breast, endometrial, prostate etc.), *inter alia*. No new matter is added by the claims herewith.

In this regard, the Examiner and SPE are directed to *Rapoport v. Dement*, 59 USPQ2d 1215 (Fed. Cir. 2001) wherein the preamble was held to be treated as a limitation, especially when used with post-transition reference thereto ("in need thereof"). That is, the Federal Circuit mandated that the USPTO MUST look for the purpose a medicament was administered in the prior art to assert anticipation or obviousness: "There is no disclosure in the FPR Publication of tests in which buspirone is administered to patients suffering from sleep apnea with the intent to cure the underlying condition." In this regard, the above-quoted recitations of claims 67 and 68 patentably distinguish the claims from the prior art, as well as from the any claims of other patents or applications of Profs. Reed and Potter or assigned to Sterix Limited. Also with respect to giving weight to the above-quoted portions of claims 67 and 68, the Examiner and SPE are also directed to *In re Wilson*, 165 USPQ 494, 496 (CCPA 1970): "All words in a claim must be considered in judging patentability of that claim against the prior art"

Furthermore, the Examiner and SPE are directed to *In re Fine*, 5 USPQ 2d 1596, 1599 (Fed. Cir. 1988) ("Obvious to try" is not the standard under 35 USC §103 and hence is not the standard under obviousness type double patenting), and to *In re Fritch*, 23 USPQ 2d 1788, 1783-1784 (Fed. Cir. 1992) ("The mere fact that the prior art may be modified in the manner suggested by the Examiner does not make the modification obvious"); *see also* In re Laskowski, 10 USPQ2d 1397, 1399 (Fed. Cir. 1989); *In re Geiger*, 2 USPQ2d 1276, 1278 (Fed. Cir. 1987). Furthermore, in examining anew the claims herewith, the Examiner and SPE are also asked to consider *In re Dow*, 5 USPQ2d 1531-1532 (Fed. Cir. 1988): "[t]here must be a reason or suggestion in the art for selecting the procedure used, other than the knowledge learned from the applicant's disclosure."

During the interviews there was also a discussion which calls to mind MPEP 2131.02 (genus can only anticipate species if species is readily envisioned from genus). In this regard, Applicants position is that the documents cited by the Examiner and SPE illustrate many OESTROGENIC compounds, and do not teach or suggest administering any specifically non-oestrogenic compound for inhibition of steroid sulphatase or for treating cancer with a steroid sulphatase inhibitor lacking intrinsic oestrogenic activity. Indeed, it seems that the Examiner and SPE make much ado about various US Patents that claim a lineage back to PCT/GB92/01587 (published as WO 93/05064). To really understand how the skilled person at the effective filing date of the instant application read PCT/GB92/01587 (published as WO 93/05064) and the

patents that claim a lineage therefrom – and the claims of those patents – attention is respectfully directed to US Patent No. 6,467,011 which claims a continuing status to USSN 09/111,927, now US Patent No. 6,011,024, and a further continuing status to US Patents Nos. 5,830,866 and 5,616,574, and ultimately to PCT/GB92/01587.

That is, to understand the 024 patent, the 084 patent, the 866 patent, the 574 patent and EVERY patent descended from PCT/GB92/01587, and the claims of ALL of those patents – as well as the disclosure of all of those patents – the Examiner and SPE are directed to US Patent No. 6,476,011 ("the '011 patent"), the cover page and claims of which are attached as Exhibit 1; and, the Examiner is respectfully requested to fully consider and make of record the '011 patent.

The 011 patent claim was fairly based on the subject matter relied upon by the Examiner and SPE. The 011 patent claims: "A method for introducing an estrogenic compound into a subject in need thereof" and the sulphamate compound being administered can be a "substituted oestrone[], … substituted oestradiol[], [or] substituted oestriol".

That is, THE USPTO HAS ALREADY INTERPRETED THE TEXT BEING RELIED UPON BY THE EXAMINER AND SPE IN THE DOUBLE PATENTING AND PREVIOUS SECTION 103 REJECTIONS AS TEACHING A METHOD FOR INTRODUCING AN ESTROGENIC COMPOUND INTO A SUBJECT, AS SHOWN BY THE ISSUANCE OF THE 011 PATENT.

Or more in particular with reference to MPEP 2131.02, the USPTO has already demonstrated by the issuance of the 011 patent that the skilled person readily envisions OESTROGENIC compounds and the administration of estrogen from that portion of PCT/GB92/01587 and the US Patents derived therefrom relied upon by the Examiner and SPE in previously rejecting claims and in asserting possible obviousness during the interviews.

In short, in view of the 011 patent, it is respectfully asserted that only but for improper hindsight gleaned from the present application can the Examiner or SPE assert that the presently claimed invention is obvious or is subject to any obviousness type double patenting rejection.

To illustrate that different patient populations as discussed during the interview indeed exist, attention is respectfully directed to the herewith enclosed article from the journal, Cancer Cell ("Selective estrogen receptor modulation: Concept and consequences in cancer" Jordan VC, Cancer Cell, March 2004, Vol.5, pages 207 to 213; "*Jordan*", copy attached as Exhibit 2, with the Examiner respectfully requested to fully consider and make of record *Jordan*).

The introduction of this article gives a background of the roles estrogens play in mediating physiological functions. Thus, in addition to affecting tumor growth, it is well known that estrogen levels affect regulation of menstruation and reproduction as well as modulate bone density and cholesterol transport.

The growth of estrogen-dependent tumors can be retarded by the administration of anti-estrogenic, selective estrogen receptor modulators (SERMs) which are widely used in clinical practice. Examples of such SERMs are tamoxifen and raloxifene.

According to the teachings of *Jordan*, breast cancer tumors can be, or become, resistant to the action of SERMs. There are two types of such resistance; intrinsic resistance and acquired resistance. Acquired resistance occurs during long-term treatment with a SERM (page 210, Figure 3) and is caused by alterations in the estrogen receptor signal transduction pathway converting the inhibitory SERM ERα complex to a growth stimulatory signal (page 210, column 2, lines 13 to 15). The combination of intrinsic and acquired resistance creates a complex survival system for the tumor.

Thus, *Jordan* teaches that there are multiple phases in the evolution of drug resistance to SERMs including a phase I where the purely antiestrogenic aromatase inhibitors can prevent tumour growth in SERM-resistant disease. This therefore represents a well-defined sub-population of patients in which the specifically non-estrogenic sulphatase inhibitors of the present invention would be indicated.

*Jordan* also teaches that with further such alteration in the estrogen receptor signal transduction pathway with continued SERM use, rather than acting as a growth stimulus for the tumour, estrogen acts as an apoptotic agent (Figure 3 of *Jordan*). In populations of patients of this type the use of non-oestrogenic sulphatase inhibitors of the present invention would clearly not be indicated. However, it is known from *Jordan* that there is therapeutic potential in such a sub-population of patients for an "estrogen purge" as tumours reoccurring after estrogen apoptosis are once again sensitive to treatment with anti-estrogens (page 211, column 1, lines 24 to 30) that would therefore be a further sub-population of patients for which the non-oestrogenic sulphatase inhibitors of the present invention would again be indicated:

> *"Laboratory studies already demonstrate that tumours that reoccur after estrogen-induced apoptosis are again sensitive to the anti-tumour actions of tamoxifen or estrogen withdrawal"*

Thus, *Jordan* teaches that there are discreet patient populations within the subset of patients with estrogen-dependent breast cancer and therefore, the presently claimed invention is directed to these discreet populations – those that require treatment or inhibition of steroid sulphatase by way of a steroid sulphatase inhibitor lacking intrinsic oestrogenic activity.

Similarly, attached is a copy of Manni, "Hormonal approaches to the chomo-prevention of endocrine-dependent tumors," Endocrine-Related Cancer (1999) 6:483-485[2] which shows at page 484, right hand column,[3] that the distinct patient population treatment, as discussed by Dr. Normanton during the 4 October 2007 interview[4] was within the art at the filing date of the instant application:

> *"Dr Malcom Pike has pioneered a different endocrine approach to the chemoprevention of hormone-dependent tumors. He and his co-workers propose to suppress ovarian function with GnRH analogue therapy and to add back low doses of estrogen and progesterone which would be insufficient to promote mammary and uterine carcinogenesis but would be high enough to provide beneficial effects such as cardiac protection and bone preservation (Spicer & Pike 1994)."*

In addition to all of the foregoing reasons for patentability, and those already of record, including the surprising results – non-oestrogenicity – demonstrated in the present application, mention is also made of the fact that foreign patent applications corresponding to the instant application have been GRANTED throughout the world, and that standards for nonobviousness and inventive step are quite similar throughout the world, especially with respect to a species that is patentably distinct from a genus. An illustration of corresponding patents granted in other jurisdictions and hence that patentability has been assessed in Applicants' favor under similar standards, submitted herewith as Exhibit 4 is a copy of the corresponding granted European Patent, EP 0 942 919 B, with the Examiner respectfully requested to consider and make this document of record too.

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[2] Copy attached as Exhibit 3, with the Examiner respectfully requested to fully consider and make this article of record; and, it is noted that this article also supports the assertion earlier-noted that the presently claimed invention is well-supported by the application and claims as originally filed.

[3] Citing Spicer & Pike, "Sex steroids and breast cancer prevention," Journal of the National Cancer Institute Monographs (1994) 16:139-147.

[4] The Examiner and SPE may recall Dr. Normanton discussing therapies involving a non-oestrogenic administration and then adding back low doses of oestrogenic compounds.

In view of the foregoing and the Exhibits hereto and the arguments of record, and the matters discussed during the interview and the claims presented herewith, reconsideration and withdrawal of the Section 112 and double patenting rejections are respectfully requested.

## REQUEST FOR INTERVIEW

If any issue remains as an impediment to allowance, prior to issuance of any paper other than a Notice of Allowance, a further interview, is respectfully requested, with the Examiner and her supervisor and the Group Director and/or a Quality Specialist, and, the Examiner is respectfully requested to contact the undersigned to arrange a mutually convenient time and manner for such an interview.

## CONCLUSION

In view of the amendments and remarks herewith, and the matters discussed during the interviews, the application is in condition for allowance. Consideration and entry of this paper, favorable reconsideration of the application, withdrawal of the rejections, withdrawal of Applicants' previous Petition (as requested at pages 1-2, above), and prompt issuance of a Notice of Allowance are earnestly solicited.

Respectfully submitted,
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